REMARKS

Claim 13 is currently pending. Claims 1-12 and 18-21 have been cancelled herewith, as directed to a non-elected invention. Claims 14-17 have also been cancelled. Claim 13 has been amended to recite a method for isolating pancreatic ducts containing proliferating pancreatic duct cells. The amendments to claim 13 are supported by the claims as originally filed and by the disclosure at page 3, lines 22-25 and page 35, lines 11-31 of the specification. No new matter is added.

Objections and Rejections

Formalities

The Examiner has objected to the title as not descriptive. Accordingly, as suggested by the Examiner, the title has been amended to better describe the invention as elected.

The Examiner has also objected to the specification for containing several informalities. As suggested by the Examiner, the specification has been amended to correct these informalities.

Claim Objections

Claims 15 and 17 have been objected to as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claims 15 and 17 have been cancelled. Therefore, this objection is moot and should be withdrawn.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 13-17 have been rejected under 35 U.S.C. § 112, second paragraph for indefiniteness. Specifically, the Examiner stated that recitation of the term "contact" renders claims 13, 15, and 17 unclear. As suggested by the Examiner, step (b) of claim 13, has been amended to recite "binding" in lieu of "the contact", thereby making step (b) consistent with step (a). Thus, this rejection should be withdrawn. Claims 14-17 have been cancelled. Therefore, this rejection, as it applies to these claims, is moot.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 13-17 have been rejected under 35 U.S.C. § 112, first paragraph for lack of enablement. According to the Examiner, detecting PDX-1+ cells as described in the

specification would not permit one to conclude that these cells are proliferating. To support this position, the Examiner cites Fernandes *et al.*, Endocrinology, 138:1750-62 (1997) ("Fernandes"), which teach that most of the pancreatic duct cells expressing PDX-1 did not proliferate. Applicants traverse.

Fernandes injected adult mice with streptozotocin (SZ), a toxin that produces hyperglycemia due to rapid and massive β cell death. Acording to the authors, one aim of this study was to ascertain whether PDX-1+ stem cells exist in adult mouse pancreas, and, if so, to ascertain whether these precursors are responsible for generation of new insulin-producing cells in diabetic animals. *See* page 1757, column 2. Fernandes reports that PDX-1+ cells were present in the pancreatic ducts of mice in their diabetic models, but that these cells were scarce and most did not proliferate, indicating that the duct is not a major source of islet precursor cells in the models of islet regeneration examined in this reference. *See* id.

Applicants contend that this finding that the pancreatic duct is not a major source of islet stem cells in SZ-treated mice, does not preclude the use of an antibody to identify PDX-1+ cells that are proliferating pancreatic duct cells in other animal systems. Specifically, Fernandes does not address the possibility that, in addition to β cell death, SZ may result in stem/progenitor cell death. The present invention does not involve the administration of a toxin before identifying PDX-1+ cells. Moreover, the specification of the present invention teaches the identification and isolation of pancreatic ducts containing proliferating pancreatic duct cells in non-SZ treated animals. *See e.g.*, Specification at page 21, lines 8-14 and page 35, lines 11-31. Thus, Applicants assert that the method recited in claim 13 is fully enabled by the specification and that this rejection should be withdrawn. Claims 14-17 have been cancelled. Therefore, this rejection, as it applies to these claims, is moot.

Claims 13 and 15-17 have been rejected under 35 U.S.C. § 112, first paragraph for lack of written description. According to the Examiner, Applicants have not adequately described the genus of reagents that bind to PDX-1. In response, claim 13 has been amended herein to identify the reagent that binds to PDX-1 is an anti-PDX-1 antibody, and claims 15-17 have been cancelled. Applicants assert that claim 13, as amended, recites subject matter which is described in the specification in such a way as to reasonably convey to one skilled in the art that the

inventors had possession of the invention at the time of filing. Therefore, this rejection should be withdrawn.

Rejection under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph

Claims 13-17 have been rejected under 35 U.S.C. § 101 as not supported by either a specific and substantial asserted utility or a well established utility. According to the Examiner, Applicants have not disclosed a use for the knowledge that there are proliferating pancreatic duct cells in a pancreatic duct. Applicants traverse.

As noted, claim 13 has been amended to recite a method for isolating pancreatic ducts containing proliferating pancreatic duct cells. In addition to contacting a pancreatic duct with an antibody that binds to PDX-1 and detecting the binding, this claim, as amended, also recites the isolation of pancreatic ducts that bind to the antibody. Such isolated, purified, and viable pancreatic ducts can then be transplanted into syngeneic recipients in order to provide purified stem/progenitor cells common to pancreatic cells and liver cells. *See* Specification, Example 5 at page 35, line 11 to page 36, line 5. Moreover, the stem/progenitor cells described in Example 5 can also be used to reconstitute pancreatic islets or hepatocytes. For example, Example 6 describes how purified duct cells were placed at ectopic sites in syngeneic recipients *in vivo* to generate new pancreatic islets or hepatocytes. *See* Specification, Example 6 at page 36, line 10 to page 37, line 21.

Therefore, Applicants contend that the use of isolated pancreatic ducts containing proliferating PDX-1+ cells, which include stem/progenitor cells common to pancreatic cells and to liver cells, in order to reconsititute pancreatic islets or hepatocytes, as described in the specification, is a specific and substantial utility. Thus, claim 13 satisfies the utility requirement, and Applicants contend that this rejection should be withdrawn. Moreover, claims 14-17 have been cancelled. Thus, this rejection, as it applies to these claims, is moot.

Claims 13-17 have also been rejected under 35 U.S.C. § 112, first paragraph because one skilled in the art would not know how to use the claimed invention. As discussed above, the claimed invention is supported by a specific and substantial asserted utility. Therefore, Applicants assert that one skilled in the art would know how to use the claimed invention. Thus, this rejection should be withdrawn.

Rejection under 35 U.S.C. § 102(b)

Claims 13-17 have been rejected under 35 U.S.C. § 102(b) as being anticipated by O'Reilly *et al.*, Diabetes, 46:599 (1997) ("O'Reilly"). According to the Examiner, O'Reilly teach the immunohistochemical detection of IPF-1 in the proliferating pancreatic duct of diabetic NOD mice. Applicants traverse.

As noted, claim 13 has been amended to recite a method for isolating pancreatic ducts containing proliferating pancreatic duct cells. In addition to contacting a pancreatic duct with an antibody that binds to PDX-1 and detecting the binding, the claim, as amended, also involves isolating the identified pancreatic duct. O'Reilly does not teach isolating those pancreatic ducts that bind to the anti-PDX-1 antibody. As noted, those ducts that bind to the anti-PDX-1 contain proliferating pancreatic duct cells that are stem/progenitor cells common to pancreatic cells and liver cells.

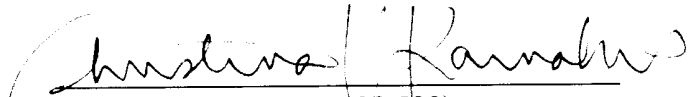
Moreover, O'Reilly teaches that the cells bearing the IPF-I marker were ductal progenitors found within the pancreatic ductal epithelia. In contrast, the stem/progenitor cells common to pancreatic cells and liver cells described by the Applicants are bipotential cells capable of differentiating into pancreatic cells and liver cells. *See* Specification at page 4, lines 14-18.

Thus, O'Reilly cannot anticipate amended claim 13 because the reference does not teach all of the elements of this claim. Accordingly, this rejection should be withdrawn. Moreover, claims 14-17 have been cancelled. Therefore, this rejection, as it applies to these claims, is moot.

CONCLUSION

On the basis of the foregoing, Applicants respectfully request that the rejection of the pending claims be withdrawn. If there are any questions regarding these remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



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